Development; Genetics; Microbiology; Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Miscellaneous Descriptors
DNA **BINDING** PROTEIN ASSOCIATION; INFECTED CELL PROLIFERATION RATE REGULATION; NUCLEOSOMAL ORGANIZATION; TRANSCRIPTION; UPSTREAM REGULATORY REGION ENHANCER

ORGANISM: Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Papovaviridae: Viruses

ORGANISM: Organism Name
Hominidae (Hominidae); Papovaviridae (Papovaviridae)

ORGANISM: Organism Superterms
animals; chordates; humans; mammals; microorganisms; primates; vertebrates; viruses

L1 ANSWER 6 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1989:164062 BIOSIS

DOCUMENT NUMBER: BA87:86163

TITLE: CONFORMATIONALLY RESTRICTED AND CONFORMATIONALLY DEFINED TYRAMINE ANALOGUES AS INHIBITORS OF PHENYLETHANOLAMINE N METHYLTRANSFERASE.

AUTHOR(S): YE Q; GRUNEWALD G L

CORPORATE SOURCE: DEP. OF MED. CHEM., UNIV. OF KANSAS, LAWRENCE, KANSAS 66045.

SOURCE: J MED CHEM, (1989) 32 (2), 478-486.
CODEN: JMCMAR. ISSN: 0022-2623.

FILE SEGMENT: BA; OLD

LANGUAGE: English

ABSTRACT:
In a search for a selective inhibitor for the epinephrine synthesizing ***enzyme*** phenylethanolamine N-methyltransferase (PNMT;EC 2.1.1.28), phenolic 2-aminotetralins (12-15 as conformationally restricted analogues of tyramine) and phenolic benzobicyclio[3.2.1]octylamines (22-24 as conformationally defined analogues of tyramine) were used to gain information about the **binding** interactions of the catecholic hydroxyl groups in the natural substrate norepinephrine at the active site of PNMT. In addition, these analogues provided information about the effects of conformational flexibility on active-site interaction of the aminoethyl side chain in phenolic phenylethylamines that may aid in learning the manner in whic norepinephrine binds at the active site of PNMT. Analogues 22-24 were synthesized by a nine-step sequence, in which a Friedel-Crafts type intramolecular cyclization was the key step in the construction of the benzobicyclo[3.2.1]octane skeleton. p-Tyramine (10, Ki = 294 uM) was more potent than phenylethylamine (1, Ki = 854 uM) but m-tyramine (9, Ki = 1250 uM) was less potent than phenylethylamine as an inhibitor of PNMT. Similarly, in the conformationally restricted and conformationally defined tyramine analogues (12-15 and 22-24, respectively), the analogues with the p-tyramine moiety (14, Ki = 4.7 uM;23, Ki = 111 uM) bind to PNMT better than do the corresponding unsubstituted compounds (16, Ki = 6.8 uM;25, Ki = 206 uM) while the analogues with the m-tyramine moiety (13, 15, 22, and 24) have a lower **binding** affinity than do 16 and 25. The greatly enhanced activity of the phenolic 2-aminotetralins (12-15) compared with m- and p-tyramine (9 and 10, respectively) is likely due to the ***restriction*** of the side-chain conformation. The conformationally defined analogues 22-24 were less active than the conformationally restricted ones, 12-15, although the low-energy half-chair conformation of 2-aminotetralin is defined in 22-24. The reduced activity of 22-24 compared with the activity of 12-15 is probably due to the **steric** hindrance from the extra bridging atoms in **binding** to PNMT. The interaction of the p-hydroxyl group of the tyramine moiety may involve hydrogen bonding since the corresponding methyl ethers show a greatly reduced affinity for the active site of PNMT (Ki = 34 and 389 uM for methoxy analogues 28 and 35, compared to Ki = 4.7 and 111 uM for the corresponding phenolic analogues 14 and 23).

CONCEPT CODE: Comparative Biochemistry, General *10010
Biochemical Studies - Proteins, Peptides and Amino Acids

10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Physiological Studies *10808
Endocrine System - Neuroendocrinology *17020
Nervous System - Physiology and Biochemistry *20504
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Neuropharmacology *22024

INDEX TERMS: Miscellaneous Descriptors
P TYRAMINE PHENYLETHYLAMINE M TYRAMINE **ENZYME** INHIBITOR-DRUG

REGISTRY NUMBER: 51-67-2 (P TYRAMINE)
64-04-0 (PHENYLETHYLAMINE)
588-05-6 (M TYRAMINE)
9037-68-7 (PHENYLETHANOLAMINE N METHYLTRANSFERASE)

L1 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1988:158753 BIOSIS
DOCUMENT NUMBER: BA85:82406
TITLE: CONFORMATIONAL AND **STERIC** ASPECTS OF THE INHIBITION OF PHENYLETHANOLAMINE N METHYLTRANSFERASE BY BENZYLAMINES.
AUTHOR(S): GRUNEWALD G L; SALL D J; MONN J A
CORPORATE SOURCE: DEP. MED. CHEM., UNIV. KANSAS, LAWRENCE, KANS. 66045.
SOURCE: J MED CHEM, (1988) 31 (2), 433-444.
CODEN: JMCMAR. ISSN: 0022-2623.
FILE SEGMENT: BA; OLD
LANGUAGE: English
ABSTRACT:
Compounds of the benzylamine (BA) class are potent inhibitors of phenylethanolamine N-methyltransferase (PNMT, EC 2.1.1.28). **Restriction** of the aminomethyl side chain through its incorporation into a cyclic framework as in 1,2,3,4-tetrahydroisoquinoline (THIQ) or 2,3,4,5-tetrahydro-1H-2-benzazepine (THBA) results in enhanced potency as an inhibitor, suggesting a conformational effect in the **binding** of BAs to the active site; however, these ring systems still retain a high degree of flexibility. We have synthesized a series of conformationally defined analogues of benzylamine in order to probe the effect of conformation, as well as the influence of ***steric*** bulk, on PNMT inhibition by this class of ligands. In addition, 1-, 3-, and 4-methyl-substituted THIQs were synthesized and evaluated as flexible models for **steric** bulk tolerance about this ring system. Substitution by a methyl group on either benzylic position of THIQ results in diminished activity as a PNMT inhibitor; however, 3-methyl-THIQ (11) shows enhanced activity as an inhibitor vs THIQ itself. Full conformational ***restriction*** of the BA side chain in analogues 4-8 results in a dramatic loss in inhibitor potency. We attribute this effect to a negative ***steric*** interaction between the alkyl bridging units above (or below) the heterocyclic ring systems and an active-site residue. Conformational ***restriction*** of THIQ employing a bridging unit that is not located above (or below) the ring system (9) results in only slightly diminished activity compared to THIQ itself. The relative activities of 4-8 were examined in terms of the conformational descriptors .tau.1 and .tau.2. Although there is no correlation between .tau.1 and activity as a PNMT inhibitor, a qualitative relationship between .tau.2 (endo or exo) and activity with PNMT is apparent. We believe that the **binding** of the N-H and/or N-lone pair of electrons may influence the spatial orientation of these molecules at the active site, resulting in positive **binding** interactions for compounds 4 and 8 and negative interactions for analogues 5-7. The results from the current investigation are compared to those obtained from a similar study involving conformationally defined amphetamines.
CONCEPT CODE: Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids

L4 ANSWER 3 OF 90 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:496360 BIOSIS
DOCUMENT NUMBER: PREV199799795563
TITLE: Sequence-specific interactions in the **Tus**-Ter complex and the effect of base pair substitutions on arrest of DNA replication in Escherichia coli.
AUTHOR(S): Coskun-Ari, Fatma Filiz; Hill, Thomas M. (1)
CORPORATE SOURCE: (1) Dep. Microbiol. Immunol., Univ. N.D. Sch. Med. Health Sci., Grand Forks, ND 58202-9037 USA
SOURCE: Journal of Biological Chemistry, (1997) Vol. 272, No. 42, pp. 26448-26456.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: **English**
ABSTRACT:
Arrest of DNA replication in Escherichia coli is mediated by specific interactions between the **Tus** protein and terminator (Ter) sequences. Binding of **Tus** to a Ter site forms a asymmetric protein-DNA complex that arrests DNA replication in an orientation-dependent fashion. In this study, mutant Ter sites carrying single base pair substitutions at 16 different positions were examined for their ability to bind purified **Tus** protein and arrest DNA replication. In vitro competition assays demonstrated that base pair substitutions at positions 8-19 had significant effects on the free energy of **Tus** binding (DELTA-DELTA-G-0 of 1.5 to gt 4.0 kcal/mol). Concomitant with loss of binding affinity, mutations at these positions also showed significantly lower or undetectable replication arrest activities in vivo. Substitutions at positions 6, 20, and 21 had moderate effects on **Tus**-Ter interactions, suggesting that these base pairs contribute to, but are not absolutely critical for, **Tus** binding. Even though the effects on binding were minimal, these Ter mutants were not as efficient as wild type **Tus**-TerB complexes at arresting replication forks. Three new potential Ter sites, referred to as TerH, TerI, and TerJ, were identified by searching the E. coli genome for sequence similarity to a consensus Ter site sequence.
CONCEPT CODE: Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Replication, Transcription, Translation *10300
Physiology and Biochemistry of Bacteria *31000
BIOSYSTEMATIC CODE: Enterobacteriaceae *06702
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Molecular Genetics (Biochemistry and Molecular Biophysics); Physiology
INDEX TERMS: Miscellaneous Descriptors
BIOCHEMISTRY AND BIOPHYSICS; DNA; REPLICATION; TERMINATOR SEQUENCE; **TUS** PROTEIN
ORGANISM: Super Taxa
Enterobacteriaceae: Eubacteria, Bacteria
ORGANISM: Organism Name
Escherichia coli (Enterobacteriaceae)
ORGANISM: Organism Superterms
bacteria; eubacteria; microorganisms

INDEX TERMS: Miscellaneous Descriptors
EC 2.1.1.28
REGISTRY NUMBER: 9037-68-7 (PHENYLETHANOLAMINE N-METHYLTRANSFERASE)
9037-68-7 (EC 2.1.1.28)

L1 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1986:207243 BIOSIS
DOCUMENT NUMBER: BA81:98543
TITLE: RECOGNITION SCHEMES FOR PROTEIN-NUCLEIC-ACID INTERACTIONS.
AUTHOR(S): GOVIL G; KUMAR N V; KUMAR M R; HOSUR R V; ROY K B; MILES H T
CORPORATE SOURCE: TATA INSTITUTE OF FUNDAMENTAL RESEARCH, BOMBAY 400 005, INDIA.
SOURCE: J BIOSCI (BANGALORE), (1985 (RECD 1986)) 8 (3-4), 645-656. CODEN: JOBSDN. ISSN: 0250-4774.
FILE SEGMENT: BA; OLD
LANGUAGE: English
ABSTRACT:
The molecular forces involved in protein-nucleic acid interaction are electrostatic, stacking and hydrogen-bonding. These interactions have a certain amount of specificity due to the directional nature of such interactions and the spatial contributions of the **steric** effects of different substituent groups. Quantum chemical calculations on these interactions have been reported which clearly bring out such features. While the **binding** energies for electrostatic interactions are an order of magnitude higher, the differences in interaction energies for structures stabilised by hydrogen-bonding and stacking are relatively small. Thus, the molecular interactions alone cannot explain the higly specific nature of **binding** observed in certain segments of proteins and nucleic acids. It is therefore logical to assume that the sequence dependent three dimensional structures of these molecules help to place the functional groups in the correct geometry for a favorable interaction between the two molecules. We have carried out 2D-FT nuclear magnetic resonance studies on the oligonucleotide d-GGATCCGGATCC. This oligonucleotide sequence has two **binding** sites for the ***restriction*** **enzyme** Bam H1. Our studies indicate that the conformation of this DNA fragment is predominantly B-type except near the ***binding*** sites where the ribose ring prefers a 3E conformation. This interesting finding raises the general question about the presence of specificity in the inherent backbone structures of proteins and nucleic acids as opposed to specific intermolecular interactions which may induce conformational changes to facilitate such **binding**.
CONCEPT CODE: Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques 10504
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Chemical and Physical *10806
Physiology and Biochemistry of Bacteria 31000
INDEX TERMS: Miscellaneous Descriptors
BAM-H-I **RESTRICTION** ENDONUCLEASE BINDIN SITE
BACKBONE STRUCTURE SPECIFICITY ELECTROSTATIC STACKING
HYDROGEN BONDING
REGISTRY NUMBER: 9055-11-2 (ENDONUCLEASE)
81295-09-2 (BAM-H-I)

L1 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1984:253438 BIOSIS
DOCUMENT NUMBER: BA77:86422
TITLE: DIRECT EVIDENCE FOR THE PREFERENTIAL **BINDING** OF ESCHERICHIA-COLI RNA POLYMERASE HOLO **ENZYME** TO THE ENDS OF DNA **RESTRICTION** FRAGMENTS.
AUTHOR(S): MELANCON P; BURGESS R R; RECORD M T JR

L4 ANSWER 4 OF 90 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:319859 BIOSIS
DOCUMENT NUMBER: PREV199799610347
TITLE: Inactivation of the replication-termination system affects the replication mode and causes unstable maintenance of plasmid R1.
AUTHOR(S): Krabbe, Margareta; Zabielski, Jan; Bernander, Rolf; Nordstrom, Kurt (1)
CORPORATE SOURCE: (1) Dep. Microbiol., Uppsala Univ., Biomed. Cent., Box 581, S-751 23 Uppsala Sweden
SOURCE: Molecular Microbiology, (1997) Vol. 24, No. 4, pp. 723-735. ISSN: 0950-382X.
DOCUMENT TYPE: Article
LANGUAGE: **English**
ABSTRACT:
Two so-called Ter sites, which bind the Escherichia coli **Tus** protein, are located near the replication origin of plasmid R1. Inactivation of the ***tus*** gene caused a large decrease in the stability of maintenance of the R1 mini-derivative pOU47 despite the presence of a functional partition system on the plasmid. Deletion of the right Ter site caused a drop in stability similar to that observed after inactivation of the **tus** gene. Substitution of 2bp required for **Tus** binding also caused unstable plasmid maintenance, whereas no effects on stability were observed when the left Ter site was deleted. Inactivation of the **tus** gene was coupled to an increased occurrence of multimeric plasmid forms as shown by gel electrophoresis of pOU47 DNA. Inactivation of the recA gene did not increase plasmid stability, suggesting that the multimerization was not mediated by RecA. Plasmid DNA was isolated from the **tus** strain carrying plasmid pOU47 and from a wild-type strain carrying pOU47 in which the right Ter site had been inactivated; in both cases, electron microscopy revealed the presence of multimers as well as rolling-circle structures with double-stranded tails. Thus, the right Ter site in plasmid R1 appears to stabilize the plasmid by preventing multimerization and shifts from theta to rolling-circle replication.
CONCEPT CODE: Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Replication, Transcription, Translation *10300
Biophysics - Molecular Properties and Macromolecules *10506
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500
BIOSYSTEMATIC CODE: Enterobacteriaceae *06702
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Genetics; Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics); Physiology
INDEX TERMS: Sequence Data
nucleotide sequence
INDEX TERMS: Miscellaneous Descriptors
E. COLI; INACTIVATION; MOLECULAR GENETICS; PLASMID R1; REPLICATION MODE; REPLICATION-TERMINATION SYSTEM; ROLLING-CIRCLE REPLICATION; STRAIN-EC1005; THETA REPLICATION; **TUS** GENE
ORGANISM: Super Taxa
Enterobacteriaceae: Eubacteria, Bacteria
ORGANISM: Organism Name
Escherichia coli (Enterobacteriaceae)
ORGANISM: Organism Superterms
bacteria; eubacteria; microorganisms

L4 ANSWER 38 OF 90 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:295798 BIOSIS
DOCUMENT NUMBER: PREV199396014023
TITLE: Sensitivity of elongation factor Tu (EF-Tu) from different bacterial species to the antibiotics efrotomycin, pulvomycin and MDL 62879.
AUTHOR(S): Landini, Paolo; Bandera, Monica; Soffientini, Adolfo; Goldstein, Beth P. (1)
CORPORATE SOURCE: (1) Marion Merrell Dow Res. Inst., Lepetit Res. Center, Via R. Lepetit 34, Gerenzano Italy
SOURCE: Journal of General Microbiology, (1993) Vol. 139, No. 4, pp. 769-774.
ISSN: 0022-1287.
DOCUMENT TYPE: Article
LANGUAGE: **English**
ABSTRACT:
The sensitivity of elongation factor Tu (EF-Tu) from different species of bacteria to the EF-Tu-binding antibiotics efrotomycin, pulvomycin and MDL 62879 was tested by measuring the effect of these antibiotics on cell-free protein synthesis systems. EF-Tu from four different Gram-negative species was sensitive to all thre antibiotics. Among Gram-positive bacteria, EF-Tu of Bacillus subtilis, Staphylococcus aureus and Enterococcus faecalis was resistant to efrotomycin and less sensitive to pulvomycin than EF-Tu of Gram-negative bacteria. EF-**Tus** from streptococci were significantly less sensitive than EF-**Tus** from Gram-negative bacteria to both efrotomycin and pulvomycin. All of the EF-**Tus** were sensitive to MDL 62879. The same sensitivity pattern emerged from GDP exchange assays, performed with partially purified EF-Tu from different bacterial species and pure Escherichia coli EF-Ts. These results suggest that the site of action of MDL 62879 is more conserved among baterial species than those of effortomycin and pulvomycin. Heterogeneity of EF-**Tus** from different bacterial species was also reflected in differences in their apparent molecular masses estimated by SDS-PAGE. EF-**Tus** from the Gram-positive species had higher molecular masses than those from all but one of the Gram-negative species.
CONCEPT CODE: Comparative Biochemistry, General *10010
Biochemical Methods - Proteins, Peptides and Amino Acids 10054
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics - Molecular Properties and Macromolecules *10506
Metabolism - Proteins, Peptides and Amino Acids *13012
Physiology and Biochemistry of Bacteria *31000
Microbiological Apparatus, Methods and Media 32000
Chemotherapy - Antibacterial Agents *38504
BIOSYSTEMATIC CODE: Neisseriaceae 06507
Pseudomonadaceae 06508
Enterobacteriaceae 06702
Pasteurellaceae 06703
Gram-Positive Cocci 07700
Micrococcaceae 07702
Endospore-forming Gram-Positives *07810
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology; Physiology
INDEX TERMS: Chemicals & Biochemicals
EFROTOMYCIN; PULVOMYCIN
INDEX TERMS: Miscellaneous Descriptors
ANTIBACTERIAL-DRUG; CELL-FREE PROTEIN SYNTHESIS; MOLECULAR MASS
ORGANISM: Super Taxa

	Endospore-forming Gram-Positives: Eubacteria, Bacteria; Enterobacteriaceae: Eubacteria, Bacteria; Gram-Positive Cocci: Eubacteria, Bacteria; Micrococcaceae: Eubacteria, Bacteria; Neisseriaceae: Eubacteria, Bacteria; Pasteurellaceae: Eubacteria, Bacteria; Pseudomonadaceae: Eubacteria, Bacteria
ORGANISM:	Organism Name endospore-forming gram-positive rods and cocci (Endospore-forming Gram-Positives); gram-positive cocci (Gram-Positive Cocci); Bacillus subtilis (Endospore-forming Gram-Positives); Enterococcus faecalis (Gram-Positive Cocci); Escherichia coli (Enterobacteriaceae); Haemophilus influenzae (Pasteurellaceae); Neisseria gonorrhoeae (Neisseriaceae); Pseudomonas aeruginosa (Pseudomonadaceae); Staphylococcus aureus (Micrococcaceae)
ORGANISM:	Organism Superterms bacteria; eubacteria; microorganisms
REGISTRY NUMBER:	56592-32-6 (EFROTOMYCIN) 11006-66-9 (PULVOMYCIN)

L4 ANSWER 44 OF 90 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1992:279785 BIOSIS
DOCUMENT NUMBER: BA94:4435
TITLE: EQUILIBRIUM KINETIC AND FOOTPRINTING STUDIES OF THE **TUS**-TER PROTEIN-DNA INTERACTION.
AUTHOR(S): GOTTLIEB P A; WU S; ZHANG X; TECKLENBURG M; KUEMPEL P; HILL T M
CORPORATE SOURCE: DEP. BIOSCIENCES BIOTECHNOL., DREXEL UNIV., PHILADELPHIA, PENNSYLVANIA 19104.
SOURCE: J BIOL CHEM, (1992) 267 (11), 7434-7443.
CODEN: JBCHA3. ISSN: 0021-9258.
FILE SEGMENT: BA; OLD
LANGUAGE: **English**
ABSTRACT:
Arrest of DNA replication in the terminus region of the Escherichia coli chromosome is mediated by protein-DNA complexes composed of the **Tus** protein and 23 base pair sequences generically called Ter sites. We have characterized the in vitro binding of purified **Tus** protein to a 37-base pair oligodeoxyribonucleotide containing the TerB sequence. The measured equilibrium binding constant (KD) for the chromosomal TerB site in KG buffer (50 mM Tris-Cl, 150 mM potassium glutamate, 25.degree. C, pH 7.5, 0.1 mM dithiothretiol, 0.1 mM EDTA, and 100 .mu.g/ml bovine serum albumin) was 3.4 .times. 10-13M. Kinetic measurements in the same buffer revealed that the ***Tus*** -TerB complex was very stable, with a half-life of 550 min, a dissociation rate constant of 2.1 .times. 10-5 s-1, and an association rate constant of 1.4 .times. 108 M-1 s-1. Similar measurements of **Tus** protein binding to the TerR2 site of the plasmid R6K showed an affinity 30-fold lower than the **Tus**-TerB interaction. This difference was due primarily to a more rapid dissociation of the **Tus**-TerR2 complex. Using standard chemical modification techniques, we also examined the DNA-protein contacts of the **Tus**-TerB interaction. Extensive contacts between the **Tus** protein and the TerB sequence were observed in the highly conserved 11 base-pair "core" sequence common to all identified Ter sites. In addition, protein-DNA contact sites were observed in the region of the Ter site where DNA replication is arrested. Projection of the footprinting data onto B-form DNA indicated that the majority of the alkylation interference and hydroxyl radical-protected sites were arranged on one face of the DNA helix. We also observed dimethyl sulfate protection of 2 guanine residues on the opposite side of the helix, suggesting that part of the **Tus** protein extends around the double helix. The distribution of contacts along the TerB sequence was consistent with the functional polarity of the **Tus** -Ter complex and suggested possible mechanisms for the impediment of protein translocation along DNA.
CONCEPT CODE: Genetics and Cytogenetics - General 03502
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics - Molecular Properties and Macromolecules *10506
Physiology and Biochemistry of Bacteria 31000
Genetics of Bacteria and Viruses *31500
BIOSYSTEMATIC CODE: Enterobacteriaceae 06702
INDEX TERMS: Miscellaneous Descriptors
ESCHERICHIA-COLI CONTACT SITES DOUBLE HELIX PROTEIN TRANSLOCATION

comparative molecular modeling: analytical method

INDEX TERMS: Miscellaneous Descriptors
hydrogen-bond formation

ORGANISM: Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISM: Organism Name
human (Hominidae)

ORGANISM: Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

REGISTRY NUMBER: 71889-75-3 (5-AMIDINOINDOLE)
9002-04-4 (THROMBIN)
9002-07-7 (TRYPSIN)
9002-05-5 (FACTOR XA)
618-39-3 (BENZAMIDINE)
56-41-7Q (ALANINE)
302-72-7Q (ALANINE)

L1 ANSWER 2 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1997:202559 BIOSIS

DOCUMENT NUMBER: PREV199799501762

TITLE: Effects of 2'-substituents of the first deoxyguanosine residue in the recognition sequence on EcoRI **restriction** endonuclease activity.

AUTHOR(S): Gohda, Keigo; Matsuo, Noriyuki; Oda, Yasushi; Ikehara, Morio; Uesugi, Seiichi (1)

CORPORATE SOURCE: (1) Dep. Bioeng., Fac. Eng., Yokohama Natl. Univ., 156 Tokiwadai, Hodogaya-ku, Yokohama 240 Japan

SOURCE: Journal of Biochemistry (Tokyo), (1997) Vol. 121, No. 2, pp. 219-224.
ISSN: 0021-924X.

DOCUMENT TYPE: Article

LANGUAGE: English

ABSTRACT:
The effects of 2'-substituents of the first deoxyguanosine on EcoRI activity were examined using synthetic octadeoxynucleotides d(GG*AATTCC) containing 2'-substituted derivatives (G*), i.e., 2'-fluoro-2'-deoxyguanosine (dGfl), 2'-chloro-2'-deoxyguanosine (dGcl), and guanosine (rG). The overall structures of the octamers were very similar, as shown by CD and UV measurements, although their EcoRI reactivities were very different: 100% in 60 min for d(GGAATTCC) and d(GGflAATTCC), 5% in 24 h for d (G(rG)AATTCC), and no cleavage at all in 24 h for d(GGclAATTCC). However, the kinetics showed the octamers exhibit similar ***binding*** -affinity to the **enzyme** (10-6-10-7 M). 31P-NMR analysis suggested the modified octamers change the phosphate backbone conformation in a duplex, since an unusual downfield-shifted signal in the spectra was commonly observed for the modified octamers at low temperature (i.e., a duplex state), which was shifted upfield at high temperature (i.e., a single strand state). The order of the differences was dGcl gt rG gt dGfl-containing octamers, coinciding with that of the vdW volume of 2'-substituents (Cl gt OH gt F) and the cleavage reactivities. These findings suggest the **steric** hindrance by the 2'-substituents causes a conformational change of the phosphate backbone close to the scissile bond, and then interferes with the EcoRI reaction.

CONCEPT CODE: Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506

External Effects - Temperature as a Primary Variable *10614
Enzymes - Methods *10804
Enzymes - Chemical and Physical *10806
Enzymes - Physiological Studies *10808

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques; Physiology

INDEX TERMS: Chemicals & Biochemicals
DEOXYGUANOSINE; ENDONUCLEASE; PHOSPHORUS-31; PHOSPHATE

INDEX TERMS: Miscellaneous Descriptors
ANALYTICAL METHOD; DEOXYGUANOSINE; DNA; DNA-PROTEIN INTERACTIONS; ECORI **RESTRICTION** ENDONUCLEASE; ENZYMOLOGY; PHOSPHATE BACKBONE CONFORMATION; PHOSPHORUS-31 NMR ANALYSIS; PROTEIN; RECOGNITION SEQUENCE; SYNTHETIC OCTADEOXYNUCLEOTIDES; 2'-SUBSTITUENTS

REGISTRY NUMBER: 961-07-9 (DEOXYGUANOSINE)
9055-11-2 (ENDONUCLEASE)
7723-14-0 (PHOSPHORUS-31)
14265-44-2 (PHOSPHATE)

L1 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:478028 BIOSIS
DOCUMENT NUMBER: PREV199396111628
TITLE: **Restriction-enzyme** cleavage of DNA modified by platinum(II) complexes.
AUTHOR(S): Brabec, Viktor; Balcarova, Zdenka
CORPORATE SOURCE: Inst. Biophys., Acad. Sciences Czech Republic, Kralovopolska 135, CS-61265 Brno Czechoslovakia
SOURCE: European Journal of Biochemistry, (1993) Vol. 216, No. 1, pp. 183-187.
ISSN: 0014-2956.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
The effect of **binding** of cis-diamminedichloroplatinum(II), its trans isomer and diethylenetriaminechloroplatinum(II) chloride to DNA on the splicing effectiveness of BamHI, EcoRI and SalI **restriction** endonucleases has been determined by means of gel electrophoresis. All three platinum complexes inhibit the cleavage of linearized plasmid DNA. In addition, the three platinum complexes bound to DNA constitute a barrier across which the linear diffusion of EcoRI on DNA is difficult. We interpret these findings to mean that the splicing effectiveness of **restriction** enzymes is influenced by bifunctional and monofunctional DNA adducts of platinum via both **steric** interference and DNA conformational distortions. Whereas the platinum adducts in the **restriction** sites or in their very close proximity inhibit the cleavage, the lesions occurring a greater distance from the **restriction** site can slow down the process of the localization of recognition sequences.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Minerals *10069
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Chemical and Physical *10806
Pharmacology - General 22002
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Genetics

INDEX TERMS: Chemicals & Biochemicals
PLATINUM-(II); CIS-DIAMMINEDICHLOROPLATINUM-(II);

TRANS-DIAMMINEDICHLOROPLATINUM-(II); BAMHI; ECORI; SALI

INDEX TERMS: Sequence Data
dna sequence; molecular sequence data

ORGANISM: Super Taxa
Ascomycetes: Fungi, Plantae; Enterobacteriaceae: Eubacteria, Bacteria; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Nematoda: Aschelminthes, Helminthes, Invertebrata, Animalia

ORGANISM: Organism Name
human (Hominidae); Caenorhabditis elegans (Nematoda); Escherichia coli (Enterobacteriaceae); Saccharomyces cerevisiae (Ascomycetes)

ORGANISM: Organism Superterms
animals; aschelminths; bacteria; chordates; eubacteria; fungi; helminths; humans; invertebrates; mammals; microorganisms; nonvascular plants; plants; primates; vertebrates

REGISTRY NUMBER: 22542-10-5D (PLATINUM-(II))
15663-27-1 (CIS-DIAMMINEDICHLOROPLATINUM-(II))
14913-33-8 (TRANS-DIAMMINEDICHLOROPLATINUM-(II))
81295-09-2 (BAMHI)
80498-17-5 (ECORI)
81295-38-7 (SALI)

L1 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:298770 BIOSIS

DOCUMENT NUMBER: PREV199396016995

TITLE: Defined analyte-**enzyme** conjugates as signal generators in immunoassays.

AUTHOR(S): Paek, Se-Hwan (1); Bachas, Leonidas G.; Schramm, Willfried

CORPORATE SOURCE: (1) Reproductive Sci. Program, Univ. Michigan, 300 N. Ingalls, Ann Arbor, Michigan 48109

SOURCE: Analytical Biochemistry, (1993) Vol. 210, No. 1, pp. 145-154.
ISSN: 0003-2697.

DOCUMENT TYPE: Article

LANGUAGE: English

ABSTRACT:
We investigated the synthesis of progesterone-horseradish peroxidase (P-HRP) conjugates and products purified by affinity chromatography. The obtained preparations were characterized with an immobilized monoclonal antibody in solid-phase immunoassays. Three homogeneous P-HRP conjugates were isolated. Two preparations were identified to contain a single progesterone ligand on the ***enzyme*** molecule. A third preparation contained two progesterone ligands. We postulate that conjugation can occur at two different positions on the **enzyme**, and that the different microenvironment of the protein structure surrounding the ligand contributes to different **binding** constants of the conjugates with immunoglobulin. By comparing the effective ***binding*** constants derived from affinity chromatography and from Scatchard analysis, we have demonstrated that the divalent conjugate binds to antibody immobilized on planer surfaces only by a single attachment due to ***steric*** **restriction**. Dose-response curves for progesterone using the isolated P-HRP conjugates have been investigated and compared.

CONCEPT CODE: Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Sterols and Steroids 10067
Biophysics - General Biophysical Techniques *10504
Enzymes - Methods *10804
Immunology and Immunochemistry - General; Methods *34502

INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Methods and

Techniques
INDEX TERMS: Chemicals & Biochemicals
PROGESTERONE; PEROXIDASE
INDEX TERMS: Miscellaneous Descriptors
AFFINITY CHROMATOGRAPHY; ANALYTICAL METHOD;
PROGESTERONE=HORSERADISH PEROXIDASE CONJUGATE
REGISTRY NUMBER: 57-83-0 (PROGESTERONE)
9003-99-0 (PEROXIDASE)

L1 ANSWER 5 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:298077 BIOSIS
DOCUMENT NUMBER: PREV199396016302
TITLE: The effect of DNA methylation on gene regulation of human papillomaviruses.
AUTHOR(S): Roesl, Frank (1); Arab, Amina; Klevens, Britta; Zur Hausen, Harald
CORPORATE SOURCE: (1) Forschungsschwerpunkt Angew. Tumorvirol., Dtsch. Krebsforschungszent., Im Neuenheimer Feld 242, 6900 Heidelberg Germany
SOURCE: Journal of General Virology, (1993) Vol. 74, No. 5, pp. 791-801.
ISSN: 0022-1317.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
Integration of human papillomaviruses (HPVs) into the host genome is considered to be an early and important event in HPV-linked cervical carcinogenesis. Consequently, the viral DNA potentially becomes a target for cellular control mechanisms normally acting on the corresponding integration site. Besides resulting position effects, host-specific DNA methylation may play a functional role in HPV gene regulation. To elucidate the influence of such a kind of epigenetic modification on viral transcription, in vitro methylation studies on HPV-18 upstream regulatory region (URR)-controlled reporter plasmids were carried out. Selective methylation of the viral URR results in a down-regulation of the transcriptional activity, which can be attributed to nonrandom distribution of methyl-acceptor sites clustered within the constitutive enhancer region. In vivo competition experiments show that suppression is not directly mediated by **steric** hindrance of methyl residues with transcription factors, but rather is due to the association with methyl-CpG DNA-**binding** proteins. Using a **restriction** ***enzyme*** accessibility assay on both the DNA and chromatin levels, it could be demonstrated that, in vivo, extensively methylated viral DNA is nucleosomally organized, characteristic of transcriptionally inactive chromatin. These data suggest that DNA methylation is an important regulatory pathway in the modulation of HPV expression and as a consequence the proliferation rate of virus-infected cells.
CONCEPT CODE: Cytology and Cytochemistry - Human *02508
Genetics and Cytogenetics - Human *03508
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics - Molecular Properties and Macromolecules *10506
Metabolism - Nucleic Acids, Purines and Pyrimidines 13014
Developmental Biology - Embryology - Morphogenesis, General *25508
Genetics of Bacteria and Viruses *31500
Virology - Animal Host Viruses *33506
BIOSYSTEMATIC CODE: Papovaviridae 02616
Hominidae *86215
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology;

BSPR:
Hiasa, H. and K. J. Marians (1992) Differential inhibition of the DNA
translocation and DNA unwinding activities of DNA helicases by the Escherichia
coli Tus protein. J. Biol. Chem. 267:11379-11385.

Finally, DnaB helicase is involved in termination of DNA replication. The
terminator protein (Tus) functions to inhibit DNA translocation and unwinding
activities of DnaB helicase, causing dissociation of helicase/ssDNA template
and termination of DNA replication (Hiasa and Marians, 1992).

— Sequence Walkers. 1997. NAR 25:448

&

Gel Reverse.

— Hengen 1997. NAR 25(24). 4994.

10064
Biophysics - Molecular Properties and Macromolecules 10506
Enzymes - Chemical and Physical *10806
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003

INDEX TERMS: Miscellaneous Descriptors
ENZYME INHIBITOR-DRUG

REGISTRY NUMBER: 100-46-9D (BENZYLAMINES)
9037-68-7 (PHENYLETHANOLAMINE N METHYLTRANSFERASE)

L1 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1988:132566 BIOSIS

DOCUMENT NUMBER: BA85:67393

TITLE: CONFORMATIONAL PREFERENCE FOR THE **BINDING** OF BIARYL SUBSTRATES AND INHIBITORS TO THE ACTIVE SITE OF PHENYLETHANOLAMINE N-METHYLTRANSFERASE.

AUTHOR(S): GRUNEWALD G L; CARTER A E; SALL D J; MONN J A

CORPORATE SOURCE: DEP. MEDICINAL CHEM., UNIV. KANSAS, LAWRENCE, KANSAS 66045.

SOURCE: J MED CHEM, (1988) 31 (1), 60-65.
CODEN: JMCMAR. ISSN: 0022-2623.

FILE SEGMENT: BA; OLD

LANGUAGE: English

ABSTRACT:
We have previously described regions of **steric** bulk tolerance in the aromatic ring **binding** site of phenylethanolamine N-methyltransferase (PNMT, EC 2.1.1.28) for phenylethanolamine substrates and .alpha.-methylbenzylamine inhibitors. For bound substrates, this region is located in the vicinity of the para position of the aromatic ring, while for bound .alpha.-methylbenzylamine inhibitors, it is located in the region complementary to the meta position. In the present study, we sought to determine the preferred conformation of the biaryl portion of (m-phenylphenyl)- and (p-phenylphenyl)ethanolamine (4 and 5, respectively) as well as for m-phenyl- and p-phenyl-.alpha.-methylbenzylamine (7 and 8, respectively) for PNMT active site interactions. Planar derivatives of 4, 5, 7, and 8 were obtained through the synthesis of 2-(1-fluorenyl)-2-hydroxyethylamine (9), 2-(2-fluorenyl)-2-hydroxyethylamine (10), 1-(1-fluorenyl)ethylamine (11), and 1-(2-fluorenyl)ethylamine (12). The four fluorene derivatives were examined for in vitro activity as substrates and inhibitors of the PNMT-catalyzed reaction. As in the case of 4, 5, 7, and 8, we have observed a positional preference for the alkylamine side chain with respect to the biphenyl skeleton present in 9-12. Thus, fluorenylethanolamine 10 ("p-biphenyl") displays a Michaelis constant (Km = 26 .mu.M) that is approximately 10 times lower than that for 9 ("m-biphenyl", Km = 297 .mu.M); in the .alpha.-methylbenzylamine inhibitors, fluorenyl derivative 11 ("m-biphenyl", Ki = 4.14 .mu.M) is approximately 40 times better than 12 ("p-biphenyl", Ki = 185 .mu.M) for in vitro inhibition of PNMT. In each case, conformational **restriction** of the biaryl system present in 4, 5, 7, and 8, such that the aromatic rings are coplanar, resulted in enhanced affinity for the PNMT active site. Thus, conformational ***restriction*** of ethanolamine 5 (Km = 82 .mu.M) as in 10 (Km = 26 .mu.M) and .alpha.-methylbenzylamine 7 (Ki = 89 .mu.M) as in 11 (Ki = 4.14 .mu.M) leads, in each case, to a stronger **enzyme**-ligand dissociable complex. These results, in conjunction with others from these laboratories, indicate that the PNMT active site beyond the zone that interacts with the central aromatic ring portion of phenylethanolamine substrates and .alpha.-methylbenzylamine inhibitors is essentially a flat, hydrophobic pocket.

CONCEPT CODE: Biochemical Methods - General 10050
Biochemical Studies - General 10060
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Methods 10804
Enzymes - Chemical and Physical *10806
Enzymes - Physiological Studies 10808
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003

CORPORATE SOURCE: DEP. CHEMISTRY, UNIV. WISCONSIN-MADISON, WIS.
SOURCE: BIOCHEMISTRY, (1983) 22 (22), 5169-5176.
CODEN: BICHAW. ISSN: 0006-2960.
FILE SEGMENT: BA; OLD
LANGUAGE: English
ABSTRACT:
E. coli RNA polymerase holoenzyme forms a variety of nonpromoter complexes with DNA **restriction** fragments in experiments performed with the nitrocellulose filter assay. Here, the use of this assay to investigate aspects of the weak (heparin-sensitive) interactions of RNA polymerase core and holoenzyme with a 1600 base pair (bp) fragment of phage T7 DNA which contains no promoters or TB (tight **binding**; heparin-resistant) sites is reported. Under the ionic conditions investigated [50 mM NaCl/10 mM MgCl2/10 mM sodium N-(2-hydroxyethyl)piperazine-N'-ethanesulfonic acid (pH 7.7)], both core and holoenzyme bind to the linear DNA fragment and cause comparable levels of filter reaction. When the DNA fragment is self-ligated into a circular molecule (non-supercoiled), the extent of **binding** of holoenzyme (but not that of core) is dramatically reduced. This directly proves previous hypotheses that holoenzyme recognizes and preferentially binds to the ends of DNA fragments and that this mode of **binding** is responsible for most of the heparin-sensitive filter retention of nonpromoter fragments. The residual mode of **binding** of holoenzyme detected with the circular DNA was considered in determining the amount of protein bound at ends only. To calculate end-**binding** constants (KE), the amount of protein bound nonspecifically (which does not appear to cause efficient filter retention) was also taken into consideration. At 0.degree. C, KE was (2.1 .+-. 0.5) .times. 108 M-1, in good agreement with that determined earlier. This value of KE is relatively constant over the temperature range 0.degree.-37.degree. C. The magnitude of KE indicates that ends can effectively compete with some promoters for RNA polymerase. Therefore, for in vitro promoter **binding** studies where **enzyme** is not in excess, end **binding** (like nonspecific **binding**) must be considered in the analysis of the promoter **binding** data, as discussed earlier. The apparent greater specificity for DNA ends of holoenzyme relative to core polymerase is discussed in terms of a **steric** model in which the .sigma. subunit helps to reduce the affinity of holoenzyme for interior DNA sites through unfavorable ***steric*** contacts that are absent in an end complex.
CONCEPT CODE: Biochemical Methods - Nucleic Acids, Purines and Pyrimidines 10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Minerals 10069
Replication, Transcription, Translation 10300
Biophysics - General Biophysical Techniques 10504
Biophysics - Molecular Properties and Macromolecules *10506
External Effects - Temperature as a Primary Variable - Cold 10616
Enzymes - Methods 10804
Enzymes - Chemical and Physical *10806
Temperature: Its Measurement, Effects and Regulation - General Measurement and Methods 23001
Temperature: Its Measurement, Effects and Regulation - Cryobiology 23004
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses 31500
Virology - Bacteriophage 33504
BIOSYSTEMATIC CODE: Pedoviridae 02145
Enterobacteriaceae 04810
INDEX TERMS: Miscellaneous Descriptors
PHAGE T-7
REGISTRY NUMBER: 9014-24-8 (RNA POLYMERASE)

L1 ANSWER 1 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:432726 BIOSIS
DOCUMENT NUMBER: PREV199900432726
TITLE: Comparative molecular modeling analysis of 5-amidinoindole and benzamidine **binding** to thrombin and trypsin: Specific H-bond formation contributes to high 5-amidinoindole potency and selectivity for thrombin and factor Xa.
AUTHOR(S): Zhou, Yasheen; Johnson, Michael E. (1)
CORPORATE SOURCE: (1) Center for Pharmaceutical Biotechnology and Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago, 833 South Wood St (m/c 874), Chicago, IL, 60612-7230 USA
SOURCE: Journal of Molecular Recognition, (July Aug., 1999) Vol. 12, No. 4, pp. 235-241.
ISSN: 0952-3499.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The coagulation cascade enzymes thrombin and factor Xa are known to have specificity pockets very similar to those of trypsin and plasmin. However, comparative molecular modeling analysis of the crystal structures of benzamidine-thrombin and benzamidine-trypsin, in conjunction with a docking analysis of 5-amidinoindole and related inhibitors in both enzymes reveals subtle differences between the specificity sites of the two types of enzymes. Specifically, thrombin and factor Xa, which have an alanine residue at position 190, exhibit increased activities for the rigid and more bulky bicyclic derivatives of benzamidine (e.g. amidinobenzofuran, amidinothiophene and amidinoindole), because of additional hydrophobic and H-bond interactions between the inhibitors and the specificity sites, whereas enzymes with a serine residue at position 190, like trypsin and plasmin, exhibit little difference in activity among the same set of compounds because of the orientational ***restriction*** imposed on the inhibitors by Ser190, which forms an additional H-bond with the amidino group of the inhibitors. Enzymes of both groups show similar responses to the flexible aminobenzamidine since the smaller size and the rotatable anilino group of the inhibitor would allow the inhibitor to achieve favorable electrostatic interactions with both groups of enzymes. 5-Amidinoindole is the most dramatic example of the rigid bicyclic type inhibitor. Based on our docking analysis, we propose that a selective H-bond with the hydroxyl group of the catalytic Ser195 and the subtle differences in **steric** fit imposed by Ala/Ser at position 190 explain the high potency and selectivity of 5-amidinoindole for thrombin and factor Xa.
CONCEPT CODE: Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Enzymes - General and Comparative Studies; Coenzymes *10802
Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
BIOSYSTEMATIC CODE: Hominidae 86215
INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Models and Simulations (Computational Biology)
INDEX TERMS: Chemicals & Biochemicals
alanine residue: position 190; benzamidine-thrombin: crystal structures; benzamidine-trypsin: crystal structures; benzamidine: **binding** characteristics; factor Xa: coagulation cascade **enzyme**, specificity pockets; thrombin: coagulation cascade **enzyme**, specificity pockets; 5-amidinoindole: **binding** characteristics
INDEX TERMS: Methods & Equipment

beta-globin gene (Mammalia)

INDEX TERMS: Methods & Equipment
DNA sequencing: Recombinant **DNA** Technology, sequencing method, sequencing techniques; PCR [polymerase chain reaction]: **DNA** amplification, amplification method, in-situ recombinant gene expression detection, sequencing techniques

ORGANISM: Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISM: Organism Name
human (Hominidae)

ORGANISM: Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L3 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1990:425867 BIOSIS

DOCUMENT NUMBER: BA90:86668

TITLE: **MOLECULAR** MODELLING STUDY OF CHANGES INDUCED BY NETROPSIN **BINDING** TO NUCLEOSOME CORE PARTICLES.

AUTHOR(S): PEREZ J J; PORTUGAL J

CORPORATE SOURCE: DEPARTAMENTO DE BIOQUIMICA Y FISILOGIA, UNIVERSIDAD DE BARCELONA, FACULTAD DE QUIMICA, DIAGONAL 647, 08028 BARCELONA, SPAIN.

SOURCE: NUCLEIC ACIDS RES, (1990) 18 (13), 3731-3738.
CODEN: NARHAD. ISSN: 0305-1048.

FILE SEGMENT: BA; OLD

LANGUAGE: English

ABSTRACT:
It is well known that certain sequence-dependent modulators in structure appear to determine the rotational positioning of **DNA** on the nucleosome core particle. That preference is rather weak and could be modified by some ligands as netropsin, a minor-groove **binding** antibiotic. We have undertaken a ***molecular*** modelling approach to calculate the relative energy of interaction between a **DNA** molecule and the **protein** core particle. The histones particle is considered as a distribution of positive charges on the **protein** surface that interacts with the **DNA** molecule. The **molecular** electrostatic potentials for the **DNA** , simulated as a discontinuous cylinder, were calculated using the values for all the base pairs. **Computing** these parameters, we calculated the relative energy of interaction and the more stable rotational setting of ***DNA*** . The **binding** of four molecules of netropsin to this model showed that a new minimum of energy is obtained when the **DNA** turns toward the **protein** surface by about 180.degree., so a new energetically favoured structure appears where netropsin **binding** sites are located facing toward the histones surface. The effect of netropsin could be explained in terms of an induced change in the phasing of **DNA** on the core particle. The induced rotation is considered to optimize non-bonded contacts between the netropsin molecules and the **DNA** backbone.

CONCEPT CODE: Cytology and Cytochemistry - General *02502
Genetics and Cytogenetics - General *03502
Mathematical Biology and Statistical Methods *04500
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Biocybernetics *10515
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014

INDEX TERMS: Miscellaneous Descriptors

DNA POSITIONING **PROTEIN** CORE PARTICLE

analytical method; viscometry: Analysis/Characterization Techniques: CB, analytical method

INDEX TERMS: Miscellaneous Descriptors
domain-domain interaction

ORGANISM: Super Taxa
Myxophyta: Fungi, Plantae; Sarcodina: Protozoa, Invertebrata, Animalia

ORGANISM: Organism Name
Dictyostelium discoideum (Myxophyta, Sarcodina)

ORGANISM: Organism Superterms
Animals; Fungi; Invertebrates; Microorganisms; Nonvascular Plants; Plants; Protozoans

L3 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:14281 BIOSIS
DOCUMENT NUMBER: PREV200000014281
TITLE: Comparison of five methods for finding conserved sequences in multiple alignments of gene regulatory regions.
AUTHOR(S): Stojanovic, Nikola; Florea, Liliana; Riemer, Cathy; Gumucio, Deborah; Slightom, Jerry; Goodman, Morris; Miller, Webb; Hardison, Ross (1)
CORPORATE SOURCE: (1) Department of Biochemistry and Molecular Biology, 206 Althouse Laboratory, Pennsylvania State University, University Park, PA, 16802 USA
SOURCE: Nucleic Acids Research, (Oct. 1, 1999) Vol. 27, No. 19, pp. 3899-3910.
ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Conserved segments in **DNA** or **protein** sequences are strong candidates for functional elements and thus appropriate methods for ***computing*** them need to be developed and compared. We describe five methods and computer programs for finding highly conserved blocks within previously computed multiple alignments, primarily for **DNA** sequences. Two of the methods are already in common use; these are based on good column agreement and high information content. Three additional methods find blocks with minimal evolutionary change, blocks that differ in at most k positions per row from a known center sequence and blocks that differ in at most k positions per row from a center sequence that is unknown a priori. The center sequence in the latter two methods is a way to model potential **binding** sites for known or unknown proteins in **DNA** sequences. The efficacy of each method was evaluated by analysis of three extensively analyzed regulatory regions in mammalian beta-globin gene clusters and the control re gion of bacterial arabinose operons. Although all five methods have quite different theoretical underpinnings, they produce rather similar results on these data sets when their parameters are adjusted to best approximate the experimental data. The optimal parameters for the method based on information content varied little for different regulatory regions of the beta-globin gene cluster and hence may be extrapolated to many other regulatory regions. The programs based on maximum allowed mismatches per row have simple parameters whose values can be chosen a priori and thus they may be more useful than the other methods when calibration againts known functional sites is not available.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Biochemical Methods - General *10050
Biochemical Studies - General *10060
BIOSYSTEMATIC CODE: Mammalia - Unspecified 85700
INDEX TERMS: Major Concepts
Molecular Genetics (Biochemistry and **Molecular** Biophysics); Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
DNA; gene regulatory regions: conserved sequences; **protein**: sequencing; mammal

Bacteria; Eubacteria; Microorganisms
REGISTRY NUMBER: 9028-86-8 (ALDEHYDE DEHYDROGENASE)

L3 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:49849 BIOSIS
DOCUMENT NUMBER: PREV200000049849
TITLE: Evidence of intramolecular regulation of the Dictyostelium discoideum 34 000 Da F-actin-bundling **protein**.
AUTHOR(S): Lim, Rita W. L.; Furukawa, Ruth; Fechheimer, Marcus (1)
CORPORATE SOURCE: (1) Department of Cellular Biology, University of Georgia, Athens, GA USA
SOURCE: Biochemistry, (Dec. 7, 1999) Vol. 38, No. 49, pp. 16323-16332.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Intramolecular interaction within the Ca2+-regulated 34 kDa actin-bundling ***protein*** from Dictyostelium discoideum was found to contribute to the regulation of its actin-**binding** activity. Recombinant N-terminally truncated proteins aa77-295, 124-295, and 139-295 bound actin at gtoreq2:1 stoichiometry, which is 5-fold greater than the intact **protein** aa1-295 as assessed by cosedimentation with F-actin. These proteins also have enhanced cross-linking activity as assessed by viscometry and electron microscopy. All truncated 34 kDa proteins failed to bind 45Ca2+ on blots and displayed Ca2+-insensitive **binding** with actin, although most proteins possessed intact putative EF-hand Ca2+-**binding** motifs. An intramolecular interaction within the 34 kDa **protein** was inferred from direct demonstrations of domain-domain interaction among the truncated 34 kDa proteins both in the presence and absence of actin. The intramolecular interaction between interaction zone 1 (aa71-123) and interaction zone 2 (aa193-254) is proposed to maintain the N-terminal inhibitory region (aa1-76) in close proximity with the strong actin-**binding** site (aa193-254) in order to modulate the interaction of the intact **protein** with actin filaments.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Cytology and Cytochemistry - General *02502
Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10502
BIOSYSTEMATIC CODE: Myxophyta 15700
Sarcodina 35300
INDEX TERMS: Major Concepts
Molecular Genetics (Biochemistry and **Molecular** Biophysics); Cell Biology; Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
F-actin bundling **protein**: analysis, **binding** activity, calcium-regulated, intramolecular regulation
INDEX TERMS: Methods & Equipment
Coomassie blue staining: staining method, staining/visualization; **Molecular** Dynamics 300A **computing** densitometer: equipment; SDS-PAGE [SDS-polyacrylamide gel electrophoresis]: gel electrophoresis, separation method; affinity coprecipitation assay: activity assays, bioassay method; affinity cosedimentation assay: activity assays, bioassay method; electron microscopy: microscopy method, microscopy: CB; polymerase chain reaction: **DNA** amplification, **DNA** amplification method, in-situ recombinant gene expression detection, sequencing techniques; scanning densitometry: Analysis/Characterization Techniques: CB,

L3 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:160175 BIOSIS
DOCUMENT NUMBER: PREV200000160175
TITLE: **Protein** patterns of gel-entrapped Escherichia coli cells differ from those of free-floating organisms.
AUTHOR(S): Perrot, Frederique; Hebraud, Michel; Charlionet, Roland; Junter, Guy-Alain; Jouenne, Thierry (1)
CORPORATE SOURCE: (1) UMR 6522 CNRS, Faculte des Sciences de Rouen, 76821, Mont-Saint-Aignan Cedex France
SOURCE: Electrophoresis., (Feb., 2000) Vol. 21, No. 3, pp. 645-653. ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The two-dimensional electrophoretic patterns of cellular proteins from gel-entrapped Escherichia coli cells were compared to those of exponential- and stationary-phase free-floating organisms. The amounts of several proteins in immobilized cells were significantly different from those in free bacteria. Immobilized organisms rapidly produced a high level of dipeptide permease and a single-strand **binding protein**, and progressively accumulated an aldehyde dehydrogenase. Immobilization also induced a decrease in the levels of two proteins, i.e., the YFID **protein** and a ***DNA*** **-binding**, stationary-phase **protein**. The possible role of these proteins in the high resistance of immobilized bacteria to stresses is discussed.
CONCEPT CODE: Biochemical Studies - General *10060
Biochemical Methods - General *10050
Bacteriology, General and Systematic *30000
INDEX TERMS: Major Concepts
Biochemistry and **Molecular** Biophysics; Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
DNA-binding protein; YFID **protein**; aldehyde dehydrogenase; cellular proteins; dipeptide permease; single-strand **binding protein**
INDEX TERMS: Methods & Equipment
Bio-Rad **protein** assay: analytical method, **protein** concentration assays; GS-700 imaging densitometer: Bio-Rad, laboratory equipment; N-terminal amino acid sequence analysis: Analysis/Characterization Techniques: CB, analytical method; ProBlott membrane: Applied Biosystems, laboratory equipment; SDS-PAGE [SDS-polyacrylamide gel electrophoresis]: polyacrylamide gel electrophoresis, separation method; autoradiography: detection method, detection/labeling techniques; centrifugation: centrifugation techniques: CB, centrifugation techniques: CT, collection method, isolation method; **computing** scanning densitometry: analytical method, photometry: CB; pulsed-liquid gas-phase sequencer: Applied Biosystems, laboratory equipment; radioactive labeling: detection/labeling techniques, laboratory equipment; two-dimensional electrophoresis: electrophoretic techniques, separation method
INDEX TERMS: Miscellaneous Descriptors
protein patterns
ORGANISM: Super Taxa
Enterobacteriaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms
ORGANISM: Organism Name
Escherichia coli (Enterobacteriaceae): free-floating, gel-entrapped
ORGANISM: Organism Superterms

L1 ANSWER 6 OF 39 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:176605 BIOSIS
DOCUMENT NUMBER: PREV199900176605
TITLE: A sticker-based model for DNA computation.
AUTHOR(S): Roweis, Sam; Winfree, Erik; Burgoyne, Richard; Chelyapov, Nickolas V.; Goodman, Myron F.; Rothemund, Paul W. K.; Adleman, Leonard M. (1)
CORPORATE SOURCE: (1) Dep. Biol. Sci., Univ. Southern California, Los Angeles, CA 90089 USA
SOURCE: Journal of Computational Biology, (Winter, 1998) Vol. 5, No. 4, pp. 615-629.
ISSN: 1066-5277.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
We introduce a new model of molecular computation that we call the sticker model. Like many previous proposals it makes use of DNA strands as the physical substrate in which information is represented and of separation by hybridization as a central mechanism. However, unlike previous models, the stickers model has a random access memory that requires no strand extension and uses no enzymes; also (at least in theory), its materials are reusable. The paper describes computation under the stickers model and discusses possible means for physically implementing each operation. Finally, we go on to propose a specific machine architecture for implementing the stickers model as a microprocessor-controlled parallel robotic workstation. In the course of this development a number of previous general concerns about molecular computation (Smith, 1996; Hartmanis, 1995; Linial et al., 1995) are addressed. First, it is clear that general-purpose algorithms can be implemented by DNA-based computers, potentially solving a wide class of search problems. Second, we find that there are challenging problems, for which only modest volumes of DNA should suffice. Third, we demonstrate that the formation and breaking of covalent bonds is not intrinsic to DNA-based computation. Fourth, we show that a single essential biotechnology, sequence-specific separation, suffices for constructing a general-purpose **molecular computer**. Concerns about errors in this separation operation and means to reduce them are addressed elsewhere (Karp et al., 1995; Roweis and Winfree, 1999). Despite these encouraging theoretical advances, we emphasize that substantial engineering challenges remain at almost all stages and that the ultimate success or failure of DNA computing will certainly depend on whether these challenges can be met in laboratory investigations.
CONCEPT CODE: General Biology - Information, Documentation, Retrieval and Computer Applications *00530
Genetics and Cytogenetics - General *03502
Mathematical Biology and Statistical Methods *04500
INDEX TERMS: Major Concepts
Mathematical Biology (Computational Biology); Models and Simulations (Computational Biology)
INDEX TERMS: Chemicals & Biochemicals
DNA: molecular computation
INDEX TERMS: Miscellaneous Descriptors
sticker model: mathematical model

L1 ANSWER 4 OF 39 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:192115 BIOSIS
DOCUMENT NUMBER: PREV200000192115
TITLE: The cell as the smallest DNA-based **molecular computer**.
AUTHOR(S): Ji, Sungchul (1)
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SOURCE: Biosystems, (Oct., 1999) Vol. 52, No. 1-3, pp. 123-133. ISSN: 0303-2647.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The pioneering work of Adleman (1994) demonstrated that DNA molecules in test tubes can be manipulated to perform a certain type of mathematical computation. This has stimulated a theoretical interest in the possibility of constructing DNA-based molecular computers. To gauge the practicality of realizing such microscopic computers, it was thought necessary to learn as much as possible from the biology of the living cell-presently the only known DNA-based ***molecular*** **computer** in existence. Here the recently developed theoretical model of the living cell (the Bhopalator) and its associated theories (e.g. cell language), principles, laws and concepts (e.g. conformons, IDS's) are briefly reviewed and summarized in the form of a set of five laws of 'molecular semiotics' (synonyms include 'microsemiotics', 'cellular semiotics', or 'cytosemiotics')-the study of signs mediating measurement, computation, and communication on the cellular and molecular levels. Hopefully, these laws will find practical applications in designing DNA-based computing systems.
CONCEPT CODE: General Biology - Information, Documentation, Retrieval and Computer Applications *00530
Cytology and Cytochemistry - General *02502
Genetics and Cytogenetics - General *03502
Mathematical Biology and Statistical Methods *04500
INDEX TERMS: Major Concepts
Computer Applications (Computational Biology); Mathematical Biology (Computational Biology)
INDEX TERMS: Miscellaneous Descriptors
DNA-based computers; cell language; cell model; conformons; cytosemiotics; microsemiotics; molecular semiotics; small DNA-based **molecular computer**